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                   and display fields
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and PCTFULL
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 NEWS 14  JUl 14   FSTA enhanced with Japanese patents
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 NEWS EXPRESS  JUNE 30 CURRENT WINDOWS VERSION IS V8.01b, CURRENT
               MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP),
               AND CURRENT DISCOVER FILE IS DATED 26 JUNE 2006.

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 NEWS X25      X.25 communication option no longer available

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=> File Medline EMBASE Biosis Caplus

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	0.42	0.42

FILE 'MEDLINE' ENTERED AT 16:03:23 ON 20 JUL 2006

FILE 'EMBASE' ENTERED AT 16:03:23 ON 20 JUL 2006

FILE 'BIOSIS' ENTERED AT 16:03:23 ON 20 JUL 2006

FILE 'CAPLUS' ENTERED AT 16:03:23 ON 20 JUL 2006

=> s (factor VII)
L1 17963 (FACTOR VII)

=> s immune (6A) glycosylation
L2 221 IMMUNE (6A) GLYCOSYLATION

=> s l1 (6A) immune
L3 18 L1 (6A) IMMUNE

=> s l1 (6A) glycosylation
L4 24 L1 (6A) GLYCOSYLATION

=> s l2 and l3 and l4
L5 0 L2 AND L3 AND L4

=> duplicate
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DUPLICATE PREFERENCE IS 'MEDLINE, EMBASE, BIOSIS, CAPLUS'
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PROCESSING COMPLETED FOR L4

L6 13 DUPLICATE REMOVE L4 (11 DUPLICATES REMOVED)

=> d l6 1-13 bib ab

L6 ANSWER 1 OF 13 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2005:1350101 CAPLUS
DN 144:102933
TI Construction and expression of human glycosylation-disrupted factor VII variants with modified pharmacokinetic properties for hemostatic use
IN Bolt, Gert; Steenstrup, Thomas Dock; Kristensen, Claus
PA Novo Nordisk Health Care AG, Switz.
SO PCT Int. Appl., 33 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005123916	A2	20051229	WO 2005-EP52834	20050617
WO 2005123916	A3	20060706		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRAI DK 2004-967 A 20040621
AB The present invention relates to human coagulation Factor VII polypeptides having modified pharmacokinetic properties, as well as polynucleotide constructs encoding such polypeptides, vectors and host cells comprising

and expressing the polynucleotide, pharmaceutical compns. comprising Factor VII polypeptides, uses and methods of treatment; and any addnl. inventive features related thereto. More specifically, the invention provides variant Factor VII polypeptides in which at least one of the two N-linked glycosylation sites present in wild-type Factor VII has been disrupted. These Factor VII variants have a decreased half-life as compared to wild-type Factor VII. The Factor VII variants of the invention can be used as hemostatics for the treatment of bleeding.

L6 ANSWER 2 OF 13 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2005:1240613 CAPLUS
DN 143:476545
TI O-linked glycoforms of polypeptides and method to manufacture them
IN Klausen, Niels Kristian
PA Novo Nordisk A/S, Den.
SO PCT Int. Appl., 56 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005111225	A1	20051124	WO 2005-EP52024	20050503

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT,

RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML,
MR, NE, SN, TD, TG
PRAI DK 2004-712 A 20040504
DK 2004-882 A 20040604
AB The present invention relates to compns. comprising glycoproteins having
altered patterns of O-linked glycosylation, in particular factor VII and factor IX, and methods for making these.
RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 3 OF 13 MEDLINE on STN DUPLICATE 1
AN 2005245611 MEDLINE
DN PubMed ID: 15616124
TI Posttranslational N-glycosylation takes place during the normal processing
of human coagulation factor VII.
AU Bolt Gert; Kristensen Claus; Steenstrup Thomas Dock
CS Mammalian Cell Technology, Novo Nordisk A/S, Novo Alle, 2880 Bagsvaerd,
Denmark.. bolt@novonordisk.com
SO Glycobiology, (2005 May) Vol. 15, No. 5, pp. 541-7. Electronic Publication: 2004-12-22.
Journal code: 9104124. ISSN: 0959-6658.
CY England: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200511
ED Entered STN: 12 May 2005
Last Updated on STN: 16 Nov 2005
Entered Medline: 15 Nov 2005
AB N-glycosylation is normally a cotranslational process that occurs during
translocation of the nascent protein to the endoplasmic reticulum. In the
present study, however, we demonstrate posttranslational N-glycosylation of recombinant human coagulation factor VII (FVII) in CHO-K1 and 293A cells. Human FVII has two N-glycosylation sites (N145 and N322). Pulse-chase labeled intracellular
FVII migrated as two bands corresponding to FVII with one and two N-glycans, respectively. N-glycosidase treatment converted both of these
band into a single band, which comigrated with mutated FVII without
N-glycans. Immediately after pulse, most labeled intracellular FVII had
one N-glycan, but during a 1-h chase, the vast majority was processed into
FVII with two N-glycans, demonstrating posttranslational N-glycosylation

of FVII. Pulse-chase analysis of N-glycosylation site knockout mutants demonstrated cotranslational glycosylation of N145 but primarily or exclusively posttranslational glycosylation of N322. The posttranslational N-glycosylation appeared to take place in the same time frame as the folding of nascent FVII into a secretion-competent conformation, indicating a link between the two processes. We propose that the cotranslational conformation(s) of FVII are unfavorable for glycosylation at N332, whereas a more favorable conformation is obtained during the posttranslational folding. This is the first documentation of posttranslational N-glycosylation of a non-modified protein in mammalian cells with an intact N-glycosylation machinery. Thus, the present study demonstrates that posttranslational N-glycosylation can be a part of the normal processing of glycoproteins.

L6 ANSWER 4 OF 13 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2004:1127523 CAPLUS
DN 142:87651
TI Human blood-coagulation factor VII or VIIa Gla domain variants and therapeutic use for bleeding disorders
IN Haaning, Jesper Mortensen; Andersen, Kim Vilbour; Bornaes, Claus
PA Maxygen Holdings Ltd., Cayman I.; Maxygen Aps
SO PCT Int. Appl., 67 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 2

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004111242	A1	20041223	WO 2004-DK428	20040618

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY,

TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM,
AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK,
EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE,
SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE,
SN, TD, TG
AU 2004247799 A1 20041223 AU 2004-247799 20040618
CA 2529828 AA 20041223 CA 2004-2529828 20040618
EP 1644504 A1 20060412 EP 2004-738925 20040618
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, HR
US 2005164932 A1 20050728 US 2004-21239 20041222
PRAI US 2003-479780P P 20030619
DK 2004-930 A 20040615
WO 2004-DK428 W 20040618
AB Gla domain variants of human factor VII or human Factor VIIa, comprising
1-15 amino acid modifications relative to human Factor VII or human Factor
VIIa, wherein a hydrophobic amino acid residue has been introduced by
substitution in position 34, or having an amino acid substitution in
position 36, or having amino acid substitutions in positions 10 and 32 and
at least one further amino acid substitution in a position selected from
74, 77 and 116.
RE.CNT 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 5 OF 13 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2002:276131 CAPLUS
DN 136:304077
TI Factor VII glycoforms having predetermined patterns of asparagine-linked
(N-linked) oligosaccharides
IN Pingel, Hans Kurt; Klausen, Niels Kristian
PA Novo Nordisk A/S, Den.
SO PCT Int. Appl., 35 pp.
CODEN: PIXXD2

DT Patent
LA English
FAN.CNT 5

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2002029025	A2	20020411	WO 2001-DK633	20011002
WO 2002029025	A3	20021010		
WO 2002029025	C2	20030515		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2422214	AA	20020411	CA 2001-2422214	20011002
AU 2001091652	A5	20020415	AU 2001-91652	20011002
US 2002137673	A1	20020926	US 2001-969357	20011002
US 6903069	B2	20050607		
US 2002151471	A1	20021017	US 2001-969358	20011002
EP 1325113	A2	20030709	EP 2001-971734	20011002
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
BR 2001014374	A	20031230	BR 2001-14374	20011002
JP 2004510786	T2	20040408	JP 2002-532595	20011002
ZA 2003002071	A	20030915	ZA 2003-2071	20030314
US 2004185534	A1	20040923	US 2003-394085	20030321
NO 2003001471	A	20030530	NO 2003-1471	20030401

US 2004058413 A1 20040325 US 2003-398422 20030902
US 2005075289 A1 20050407 US 2003-725843 20031202
PRAI DK 2000-1456 A 20001002
US 2000-238944P P 20001010
DK 2001-262 A 20010216
US 2001-271581P P 20010226
DK 2001-430 A 20010314
US 2001-276322P P 20010316
DK 2001-751 A 20010514
US 2001-969357 A1 20011002
WO 2001-DK633 W 20011002
AB The present invention relates to compns. comprising Factor VII and other blood clotting factors having altered patterns of asparagine-linked glycosylation. The present inventors have discovered that prepns. of coagulation proteins having predetd. glycoform patterns exhibit improved functional properties. Accordingly, the present invention relates to methods and compns. that provide these protein prepns. In particular, the invention relates to prepns. comprising Factor VII polypeptides and Factor VII-related polypeptides having specific predetd. patterns of asparagine-linked (N-linked) oligosaccharides. Structures were characterized as core fucosylated bi- and triantennary structures with 0-3 sialic-acid residues, which were α2-3 linked to galactose exclusively. Some of the structures had one or two galactose residues substituted by N-acetylgalactosamine. The prepns. of the invention exhibit altered properties, including, without limitation, improved pharmacokinetic properties and improved clin. efficacy. The invention also encompasses pharmaceutical formulations that comprise these prepns., as well as therapeutic methods that utilize the formulations.

L6 ANSWER 6 OF 13 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2001:598020 CAPLUS
DN 135:185436
TI Factor VII or VIIa-like molecules for treatment of blood coagulation disorders
IN Andersen, Kim Vilbour; Pedersen, Anders Hjelholt; Bornaes, Claus
PA Maxygen Aps, Den.

SO PCT Int. Appl., 89 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2001058935	A2	20010816	WO 2001-DK94	20010212
WO 2001058935	A3	20011129		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2397347	AA	20010816	CA 2001-2397347	20010212
EP 1257295	A2	20021120	EP 2001-903611	20010212
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
US 2003096338	A1	20030522	US 2001-782587	20010212
US 6806063	B2	20041019		
JP 2003521930	T2	20030722	JP 2001-558082	20010212
NZ 521257	A	20041029	NZ 2001-521257	20010212
AU 783512	B2	20051103	AU 2001-31535	20010212
RU 2278123	C2	20060620	RU 2002-124129	20010212
NO 2002003804	A	20020925	NO 2002-3804	20020809
US 2006019336	A1	20060126	US 2004-950747	20040927
JP 2005270110	A2	20051006	JP 2005-122294	20050420

AU 2006200448 A1 20060302 AU 2006-200448
20060202
PRAI DK 2000-218 A 20000211
DK 2000-1558 A 20001018
US 2000-184036P P 20000222
US 2000-241916P P 20001018
AU 2001-31535 A 20010212
JP 2001-558082 A3 20010212
US 2001-782587 A3 20010212
WO 2001-DK94 W 20010212
AB The present invention relates to novel factor VII (FVII) or Factor VIIa
(FVIIa) polypeptide conjugates, to their preparation and use in therapy, in
particular for the treatment of a variety of coagulation-related
disorders. These novel polypeptide conjugates comprise at least one
non-polypeptide moiety covalently attached to a polypeptide, wherein the
amino acid sequence of the polypeptide differs from that of wild-type FVII
or FVIIa in that at least one amino acid residue comprising an attachment
group for said non-polypeptide moiety has been introduced or removed. The
conjugates of the present invention have one or more improved properties
as compared to com. available rFVIIa, including increased functional in
vivo half-life and/or increased plasma half-life, and/or increased
bioavailability and/or reduced sensitivity to proteolytic degradation

L6 ANSWER 7 OF 13 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2001:503530 CAPLUS
DN 135:223362
TI Factor VII and single-chain plasminogen activator-activating protease:
activation and autoactivation of the proenzyme
AU Kannemeier, Christian; Feussner, Annette; Stohr, Hans-Arnold; Weisse,
Jorg; Preissner, Klaus T.; Romisch, Jurgen
CS Aventis Behring GmbH, Marburg, Germany
SO European Journal of Biochemistry (2001), 268(13), 3789-3796
CODEN: EJBCAI; ISSN: 0014-2956
PB Blackwell Science Ltd.
DT Journal
LA English
AB Structural and biol. characteristics of a recently described plasma serine
protease, which displayed factor VII as well as pro-urokinase-activating

properties in vitro, indicated a dual role for this factor VII-activating protease (FSAP) in hemostasis. Only the active protease (two-chain FSAP) has been isolated from plasma and from a prothrombin complex concentrate, whereas activators of the proenzyme have not been identified so far. After purification of the FSAP proenzyme from cryo-poor plasma by adsorption to an immobilized mAb and subsequent ion-exchange chromatog., activation to generate two-chain FSAP was followed by a direct chromogenic assay as well as by the ability of two-chain FSAP to activate pro-urokinase. Purified single-chain FSAP underwent autoactivation leading to the typical protease two-chain pattern and subsequent degradation products, as demonstrated by Western-blotting anal. using a site-specific mAb. This autoactivation was significantly enhanced in the presence of heparin, whereas Ca2+ ions stabilized single-chain FSAP (the proenzyme) resulting in slower autoactivation kinetics. Correspondingly, the heparin-augmented reaction, which was associated with autodegrdn. particularly of the protease domain, was slowed down by co-incubation with Ca2+. Of the other proteases and cofactors tested, only urokinase (uPA) was able to generate the typical two-chain FSAP pattern. Studies with different forms of uPA suggest that the catalytic activity of pro-urokinase/uPA is needed to activate single-chain FSAP, indicating that it is the only hemostatic protease that can act as a physiol. activator of FSAP.

RE.CNT 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 8 OF 13 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN

AN 2001:305264 BIOSIS

DN PREV200100305264

TI Lack of heavy chain glycosylation in patient with factor VII deficiency not responsible for mutant FVIIA activity.

AU Toso, Raffaella [Reprint author]; Tidd, Theresa [Reprint author]; Arruda, Valder [Reprint author]; High, Katherine A. [Reprint author]; Pollak,

Eleanor S. [Reprint author]
CS Research Hematology, Children's Hospital of Philadelphia, Philadelphia,
PA, USA
SO Blood, (November 16, 2000) Vol. 96, No. 11 Part 2, pp. 79b. print.
Meeting Info.: 42nd Annual Meeting of the American Society of Hematology.
San Francisco, California, USA. December 01-05, 2000. American Society of
Hematology.
CODEN: BLOOAW. ISSN: 0006-4971.
DT Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LA English
ED Entered STN: 27 Jun 2001
Last Updated on STN: 19 Feb 2002
AB We have carried out a series of FVII structure-function studies based on
naturally occurring mutations. A patient with FVII deficiency (FVII
coagulant activity 39%, FVII antigen 54%) was found to be a compound
heterozygote with two missense mutations in exon 8, one resulting in a Thr
to Met mutation at amino acid 324 (T324M) in the FVII heavy chain core
glycosylation sequence Asn-X-Thr/Ser and the other resulting in a Glu to
Lys mutation encoding amino acid 385 (E385K). Four mutant FVII proteins
were synthesized in vitro in HEK293 cells and purified on a Ca2+-dependent
immuno-affinity column. The mutant recombinant FVII proteins included
T324M, E385K and two mutant FVII proteins lacking glycosylation core
sequences in either the FVII heavy chain (N322Q) or the FVII light chain
(N145Q). Deglycosylation experiments confirmed absent glycosylation
sites. Data from in vitro experiments are shown. The T324M mutant FVII,
but no other mutant protein, shows incomplete conversion from zymogen to
the two-chain FVIIa by FVII activators (FIXa, FXa, FXIIa and TF/FVIIa).
In vivo monitoring of antigenic FVII levels showed a decreased survival of
N145Q after injection into 6 week old normal C57BL/6 mice (n=4) compared
with survival of mutants N322Q and T324M. In summary, the loss of

activity of the patient's mutant FVII can neither be explained by the absence of carbohydrate in the FVII heavy chain as shown by N322Q nor by the effect of the E385K mutation. The T324M mutation itself likely causes a conformational change in the three-dimensional structure of the protein and dramatically reduces the activity of the T324M FVIIa species and also reduces the ability of T324M to be fully activated.

L6 ANSWER 9 OF 13 MEDLINE on STN DUPLICATE 2
AN 1999282173 MEDLINE
DN PubMed ID: 10353820
TI The effect of O-fucosylation on the first EGF-like domain from human blood coagulation factor VII.
AU Kao Y H; Lee G F; Wang Y; Starovasnik M A; Kelley R F; Spellman M W; Lerner L
CS Department of Analytical Chemistry, Genentech, Inc., South San Francisco, California 94080, USA.
SO Biochemistry, (1999 Jun 1) Vol. 38, No. 22, pp. 7097-110. Journal code: 0370623. ISSN: 0006-2960.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
OS PDB-1F7E; PDB-1FF7
EM 199906
ED Entered STN: 12 Jul 1999
Last Updated on STN: 3 Mar 2000
Entered Medline: 23 Jun 1999
AB The first epidermal growth factor-like domain (EGF-1) from blood coagulation factor VII (FVII) contains two unusual O-linked glycosylation sites at Ser-52 and Ser-60. We report here a detailed study of the effect of O-fucosylation at Ser-60 on the structure of FVII EGF-1, its Ca2+-binding affinity, and its interaction with tissue factor (TF). The in vitro fucosylation of the nonglycosylated FVII EGF-1 was achieved by using O-fucosyltransferase purified from Chinese hamster ovary cells. Distance and dihedral constraints derived from NMR data were used to determine the solution structures of both nonglycosylated and fucosylated FVII EGF-1 in the presence of CaCl2. The

overall structure of fucosylated FVII EGF-1 is very similar to the nonfucosylated form even for the residues near the fucosylation site. The Ca2+ dissociation constants (Kd) for the nonfucosylated and fucosylated FVII EGF-1 were found to be 16.4 +/- 1.8 and 8.6 +/- 1.4 mM, respectively. The FVII EGF-1 domain binds to the extracellular part of TF with a low affinity (Kd approximately 0. 6 mM), and the addition of fucose appears to have no effect on this affinity. These results indicate that the FVII EGF-1 alone cannot form a tight complex with TF and suggest that the high binding affinity of FVIIa for TF requires cooperative interaction among the four domains in FVII with TF. Although the fucose has no significant effect on the interaction between TF and the individual FVII EGF-1 domain, it may affect the interaction of full-length FVIIa with TF by influencing its Ca2+-binding affinity.

L6 ANSWER 10 OF 13 CAPLUS COPYRIGHT 2006 ACS on STN
AN 1998:272213 CAPLUS
DN 129:64829
TI Functional consequences of mutations in Ser-52 and Ser-60 in human blood coagulation factor VII
AU Iino, Masaki; Foster, Donald C.; Kisiel, Walter
CS Department of Pathology, University of New Mexico School of Medicine, Albuquerque, NM, 87131, USA
SO Archives of Biochemistry and Biophysics (1998), 352(2), 182-192
CODEN: ABBIA4; ISSN: 0003-9861
PB Academic Press
DT Journal
LA English
AB Human blood coagulation factor VII has unique carbohydrate moieties O-glycosidically linked to serine 52 and serine 60 residues in its first epidermal growth factor-like domain. To study the functional role of these glycosyl moieties in factor VII, we constructed, expressed, and purified site-specific recombinant mutants of human factor VII in which serine 52 and serine 60 were conservatively replaced with alanine

residues. S52A factor VIIa (Ser-52 → Ala), S60A factor VIIa (Ser-60 → Ala), and S52,60A factor VIIa (Ser-52, Ser-60 → Ala) exhibited 56, 73, and 44%, resp., of the clotting activity of wild-type factor VIIa using human brain thromboplastin as a source of tissue factor/phospholipids and 32, 43, and 14% of wild-type factor VIIa using a mixture of recombinant soluble tissue factor and mixed brain phospholipids. The tissue factor-dependent and -independent amidolytic activities of these mutants were essentially indistinguishable from that of wild-type factor VIIa. In addition, equilibrium dialysis expts. indicated that the profiles of 45Ca2+ binding to these mutants were identical with that of wild-type factor VII. In the presence of either Ca2+ or EGTA, the Kd values for the interaction of the three factor VIIa mutants to full-length tissue factor were 2- to 5-fold higher than that of wild-type factor VIIa, while the Kd values for the interaction of these mutants to soluble tissue factor were 4- to 15-fold higher than that of wild-type factor VIIa. Measurement of the association and dissociation rate consts. for factor VIIa binding to re-lipidated tissue factor apoprotein revealed that the association rate consts. of the three factor VII mutants were decreased in comparison with that of wild-type factor VIIa, while the dissociation rate consts. of these three mutants were virtually identical to that of wild-type factor VIIa. These findings strongly suggest that glycosyl moieties attached to Ser-52 and Ser-60 in factor VII/VIIa provide unique structural elements that are important for the rapid association of factor VII/VIIa with its cellular receptor and cofactor.

RE.CNT 53 THERE ARE 53 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 11 OF 13 MEDLINE on STN DUPLICATE 3
AN 91250411 MEDLINE
DN PubMed ID: 1904059
TI Human plasma and recombinant factor VII.

Characterization of O-glycosylations at serine residues 52 and 60 and effects of site-directed mutagenesis of serine 52 to alanine.

AU Bjoern S; Foster D C; Thim L; Wiberg F C; Christensen M; Komiyama Y; Pedersen A H; Kisiel W
CS Bioscience Corporate Research, Novo Nordisk A/S, Bagsvaerd, Denmark.

NC HL 35246 (NHLBI)
SO The Journal of biological chemistry, (1991 Jun 15) Vol. 266, No. 17, pp. 11051-7.
Journal code: 2985121R. ISSN: 0021-9258.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199107
ED Entered STN: 28 Jul 1991
Last Updated on STN: 3 Feb 1997
Entered Medline: 10 Jul 1991

AB Factor VII is a multidomain, vitamin K-dependent plasma glycoprotein that participates in the extrinsic pathway of blood coagulation. Earlier studies demonstrated a novel disaccharide (Xyl-Glc) or trisaccharide (Xyl2-Glc) O-glycosidically linked to serine 52 in human plasma factor VII (Nishimura, H., Kawabata, S., Kisiel, W., Hase, S., Ikenaka, T., Shimonishi, Y., and Iwanaga, S. (1989) J. Biol. Chemical 264, 20320-20325). In the present study, human plasma and recombinant factor VII were isolated and subjected to enzymatic fragmentation. Peptides comprising residues 48-62 of the first epidermal growth factor-like domain of each factor VII preparation were isolated for comparative analysis. Using a combined strategy of amino acid sequencing, carbohydrate and amino acid composition analysis, and mass spectrometry, three different glycan structures consisting of either glucose, glucose-xylose, or glucose-(xylose)2 were detected O-glycosidically linked to serine 52 in plasma and recombinant factor VII. Approximately equal amounts of the three glycan structures were observed in plasma factor VII, whereas in recombinant factor VII the glucose and the glucose-(xylose)2 structures

predominated. In addition to the O-linked glycan structures observed at serine 52, a single fucose was found to be covalently linked at serine 60 in both human plasma and recombinant factor VII. Carbohydrate and mass spectrometry analyses indicated that the fucosylation of serine 60 was virtually quantitative. Metabolic labeling studies using [14C]fucose confirmed the presence of O-linked fucose at serine 60. In order to assess whether the carbohydrate moiety at serine 52 contributes to the biological activity of factor VII, we have constructed a site-specific mutant of recombinant factor VII in which serine 52 has been replaced with an alanine residue. Mutant factor VIIa exhibited approximately 60% of the coagulant activity of wild-type factor VIIa in a clotting assay. The amidolytic activity of mutant factor VIIa was indistinguishable from that observed for recombinant wild-type factor VIIa. In addition, the ability of mutant factor VIIa in complex with either purified relipidated tissue factor apoprotein or tissue factor on the surface of a human bladder carcinoma cell line (J82) to activate either factor X or factor IX was virtually identical to that observed for wild-type factor VIIa. These results indicate that the carbohydrate moiety O-glycosidically linked to serine 52 does not appear to be involved either in the interaction of factor VIIa with tissue factor, or the expression of its proteolytic activity toward factor X or factor IX following complex formation with tissue factor.(ABSTRACT TRUNCATED AT 400 WORDS)

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AN 1986:297055 BIOSIS

DN PREV198682030961; BA82:30961

TI APPLICATION OF FACTOR-VII-SEPHAROSE AFFINITY CHROMATOGRAPHY IN THE PURIFICATION OF HUMAN TISSUE FACTOR APOPROTEIN.

AU BOM V J J [Reprint author]; RAM I E; ALDERKAMP G H J; REINALDA-POOT H H;
BERTINA R M
CS HAEMOSTASIS THROMBOSIS RES UNIT, LEIDEN UNIV HOSPITAL, 2333 AA LEIDEN,
NETH
SO Thrombosis Research, (1986) Vol. 42, No. 5, pp. 635-644.
CODEN: THBRAA. ISSN: 0049-3848.
DT Article
FS BA
LA ENGLISH
ED Entered STN: 25 Jul 1986
Last Updated on STN: 25 Jul 1986
AB Coagulation factor VII covalently coupled to Sepharose proved to be an
effective binding ligand for human tissue factor apoprotein, the specific
cofactor of factor VII for the activation of factor X and IX. This
interaction is completely calcium-dependent and the calcium ions cannot be
replaced by magnesium or barium ions. The binding of the apoprotein to
immobolized factor VII seems to be independent of the presence of
phospholipid. When factor VII-Sepharose column chromatography is combined
with a mild extraction procedure, tissue factor apoprotein could be
purified .apprx. 40,000-fold from an acetone powder of human brain.
SDS-PAA gel electrophoresis revealed that with this simple purification
scheme human tissue factor apoprotein can be purified to apparent
homogeneity and that the apoprotein migrates at a molecular weight of
47,000. The isolated human protein is heterogeneously glycosylated; the
two different forms of the apoprotein function as cofactor of factor VII
in the activation of both factor X and factor IX.

L6 ANSWER 13 OF 13 MEDLINE on STN DUPLICATE 4
AN 85184022 MEDLINE
DN PubMed ID: 3872909
TI Modulation of the biologic activities of IgE-binding factors. VII. Biochemical mechanisms by which glycosylation -enhancing factor activates phospholipase in lymphocytes.
AU Akasaki M; Iwata M; Ishizaka K
NC AI-14784 (NIAID)
SO Journal of immunology (Baltimore, Md. : 1950), (1985 Jun) Vol. 134, No. 6,
pp. 4069-77.

Journal code: 2985117R. ISSN: 0022-1767.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Abridged Index Medicus Journals; Priority Journals
EM 198506
ED Entered STN: 20 Mar 1990
Last Updated on STN: 3 Feb 1997
Entered Medline: 20 Jun 1985
AB Cells of the T cell hybridoma 23A4 produce IgE-binding factors lacking
N-linked oligosaccharides (unglycosylated form) when they are incubated
with IgE alone. In the presence of glycosylation-enhancing factor (GEF)
or bradykinin, however, the same cells produce IgE-binding factors with
N-linked oligosaccharides (glycosylated form). Switching the cells from
the formation of unglycosylated IgE-binding factors to the formation of
glycosylated factors was accompanied by the release of both
glycosylation-inhibiting factor (GIF) in its phosphorylated form, i.e.,
phosphorylated lipomodulin, and arachidonate from the cells. Analysis of
the biochemical processes for the release of GIF from 23A4 cells showed
that affinity-purified GEF or bradykinin induced transient phospholipid
methylation and diacylglycerol (DAG) formation, and enhanced 45Ca uptake
into the cells. Inhibitors of methyltransferases, i.e., 3-deaza-adenosine
plus L-homocysteine thiolactone, inhibited not only phospholipid
methylation but also DAG formation and GIF release. Exogenously added
1-oleoyl-2-acetyl glycerol, i.e., a DAG that is permeable to the plasma
membrane, induced the release of GIF from the cells. It was also found
that 12-O-tetradecanoyl-phorbol 13-acetate (TPA) switched 23A4 cells and
normal lymphocytes to the selective formation of N-glycosylated
IgE-binding factor, and induced the release of GIF from the cells.
32PO4-labeled lipomodulin was detected in the extract of 23A4 cells 3 to 5
min after the addition of GEF, bradykinin, or TPA. These results indicate
that GEF and bradykinin induced the activation of methyltransferases and

phospholipase C for the formation of DAG, which in turn activated Ca2+-activated, phospholipid-dependent protein kinase (protein kinase C) for the phosphorylation of lipomodulin. Because lipomodulin loses phospholipase inhibitory activity after phosphorylation, increased phospholipase A2 activity would be expressed by this process.